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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,337	02/05/2004	Fumihiko Yokoya	25908	3930

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EXAMINER

WHALEY, PABLO S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,337	YOKOYA ET AL.	
	Examiner	Art Unit	
	Pablo Whaley	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 March 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) 9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 6-8 is/are rejected.
- 7) ☒ Claim(s) 4 and 5 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>3 IDS forms</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

APPLICANT'S ELECTION

Applicant's election traverse of Group I (Claims 1-8) in the reply filed on 04/20/2006 is acknowledged. Applicant's election traverse of Specie A (Gene No. 1, as recited in Table 1) is acknowledged. The traversal is on the ground(s) that the examination of Groups I and II would not be a search burden. This is not found persuasive as the gene panel of Group I is not limited to drug screening applications, as set forth in the previous office action mailed 3/20/2006, and because the examination process requires a search of non-patent literature, U.S. patent publications, U.S. patents, as well as foreign patent literature. The requirement is still deemed proper and is therefore made FINAL. Claim 9 is hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 04/20/2006.

CLAIMS UNDER EXAMINATION

Claims herein under examination are Claims 1-8 as they read on the elected species. An action on the merits follows.

INFORMATION DISCLOSURE STATEMENT

The information disclosure statements filed 8/20/04, 3/9/04, and 4/11/06 have been considered in full.

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OBJECTION

Claims 4 and 5 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 4 and 5 have not been further treated on the merits.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. Claims 1-3 are directed to a "gene panel" comprising names and gene expression profiles of genes. As the specification does not define or fully and completely describe a "gene panel" such that it is necessarily interpreted as a physical product, and as "names" and "expression profiles" are not necessarily physical elements, the "gene panel" is merely a data listing, and is not statutory subject matter.

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "names and gene expression profiles of genes each showing, in hepatic stellate cells, an increased expression level." It is unclear as to the intended meaning of "showing, in hepatic stellate cells." In this context, it cannot be determined as to exactly what is "showing" in the cells (i.e. actual genes, gene expression profiles, or something else). If applicant simply intends for gene showing "in hepatic stellate cells" to mean the actual genes or expression levels are within hepatic stellate cells, the claims should state this clearly. Clarification is requested.

Claim 2 recites the limitation "model animal." This term is indefinite as "model animal" could be interpreted to be an actual model animal (i.e. non-living), a virtual animal (i.e. simulated), an real animal (i.e. living), or otherwise. Clarification is requested.

The preamble of claim 6 recites a "method of producing a gene panel." However, as there is no step directed to "producing a gene panel" and as claim 6, step (c), results in the identification of genes, it is unclear in what way the steps of claim 6 achieve the purpose of the preamble. Clarification is requested.

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 102 (b) as being anticipated by Lawrence et al. (Proteins: Structure, Function, and Genetics, 1992, 12, p.31-41).

Lawrence et al. teach a search algorithm for finding novel therapeutic agents capable of binding proteins of known 3-D structure [Abstract], as in instant claims 1 and 2. More specifically, Lawrence et al. teach the following aspects of the instant invention:

- Databases comprising chemical and crystallographic connectivity (i.e. biological interaction) data of small organic molecules [Abstract and p.37, Col. 2, ¶ 2], as in instant claim 1.
- Probe/protein interaction-energy map data generated [p.32, Col. 2 ¶ 4], which is also a teaching for biological interaction data as in instant claim 1.
- GRID program determines favorable interaction positions (i.e. molecular target sites) in the binding site of the protein [p.32, Methods, ¶ 1], and identification of sialic acid binding site and a number of potential sialic acid-protein interactions [p.37, Col. 2, ¶ 2], which is a teaching for two or more molecular targets as in instant claims 1, 3, and 7.

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- GRID examines the chemical structure of candidate molecule [Fig. 1] and suggests chemical changes to candidate molecules that enhance binding with a target protein [p.35, col. 2, Chemical Substitutions], which correlates to identifying additional applications and uses of known compounds, as in instant claims 2 and 6.
- GRID identifies a number of new ligands to the protein associated with a mutant influenza virus [Table 1], which correlates to identification of multiple candidate compounds associated with treatment of a disease state as in instant claims 1 and 3.
- GRID selects candidates based on favorable geometric and chemical interaction with the protein binding site [p. 31, col. 2, ¶ 2], which correlates to *in silico* identification of compounds based on “patterns of activity” as in instant claim 4 and “desired activity” as in instant claim 8.
- CLIX program searches for candidate molecules from a set (L) generated by excluding molecules containing known toxic elements [p.33, Col. 1, ¶ 1 and ¶ 2], which is a teaching for selection of compounds associated with toxicity as in instant claim 5.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 103(a) as being made obvious by Zhumabayeva et al. (CLONTECHniques, April 2001, p.1-2), in view of Kristensen et al. (Hepatology, 2000, Vol. 32, No. 2, p.268-277)

Zhumabayeva et al. teach a method of temporal and differential gene expression using microarrays (i.e. gene chips) (Abstract). More specifically, Zhumabayeva et al. teach the following aspects of the instantly claimed invention:

- Microarray of gene expression (i.e. gene panel) comprising names and gene expression data showing increased expression levels [Figs. 1 and 2], as in instant claim 1. As a microarray is reasonably interpreted as a "gene chip", instant claim 8 is also anticipated.
- Increased expression levels correspond to a difference of expression levels in human tissues [Fig. 1].

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- Gene expression levels taken after overnight hybridization [p.1, Col. 3, ¶ 2], which correlates to time-varying expression as in instant claim 3.
- Measuring expression levels of various genes in normal (N) and tumor (T) states [Fig. 1], which equates to active and resting states, as in instant claim 6.
- Comparison of expression levels [p.2, ¶ 2 and ¶ 3] and identification of genes showing increased (or decreased) expression levels [Fig. 1], as in instant claim 6.

Zhumabayeva et al. do not specifically teach hepatic stellate cells or an animal model having cirrhosis and hepatic fibrosis, as in instant claim 2.

Kristensen et al. teach an animal model for the proteomic analysis of cellular and secreted proteins from rat hepatic stellate cells [Abstract]. More specifically, Kristensen et al. teach the following aspects of the instantly claimed invention:

- Liver fibrosis was induced in a rat model population [p.269, Materials and Methods, ¶ 3], as in instant claim 2. As cirrhosis (www.answers.com) is well known to be a chronic disease of the liver characterized by the replacement of normal tissue with fibrous tissue, a teaching for animals with liver (i.e. hepatic) fibrosis is inherently a teaching for animals with liver cirrhosis.
- Gene panel of expression levels from normal (quiescent) and activated hepatic stellate cells obtained over time [Fig. 2], as in instant claims 1, 2, and 3.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to combine the hepatic stellate cell protein expression data of Kristensen et al. with the gene expression profiling array information of Zhumabayeva et al., where the motivation would have been to improve gene expression profiling of liver fibrosis by using the

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rapid microarray-based method and differential profiling array taught by Zhumabayeva et al. One of ordinary skill in the art would have had a reasonable expectation of successfully combining the protein expression data of Kristensen et al. with the gene profiling array of Zhumabayeva et al. as both teach gene expression analysis of proteomic data.

CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley

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MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
7/6/06